TOBACCO SMOKE CONSTITUENTS

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I. INTRODUCTION

Tobacco smoke is a highly complex mixture containing, by some estimates, over 4,000 constituents. Over the years, much time and effort has been devoted to determining the identity of tobacco smoke constituents. This has proven difficult, however, and much remains to be learned about the structure and makeup of tobacco smoke and its relationship, if any, to human disease.

Ninety percent of cigarette smoke is air, water and carbon dioxide, a natural by-product of combustion. Of the remaining 10 percent, only a few substances such as nicotine and carbon monoxide (CO) have been measured by researchers as being present in smoke at levels above one milligram per cigarette. Anti-smoking advocates frequently assert that nicotine and CO cause disease in humans. The same is also said about "tar," even though it is a laboratory product, not an actual constituent of tobacco smoke.

The vast majority of the remaining constituents actually present in cigarette smoke, some of which have been identified in "tar," are present only in extremely small amounts, measured in micrograms (millionths of a gram) or nanograms (billionths of a gram) per cigarette. Nonetheless, anti-smoking advocates occasionally single out for public criticism certain smoke constituents other than "tar," nicotine and CO that have, under conditions and at levels vastly different from those to which a human smoker is

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exposed, been associated with disease in animals or humans. These substances, however, are ubiquitous. Smokers and non-smokers alike are exposed to most of these substances every day simply by breathing air, drinking water and eating food.

The significance of smoke constituents to human health, if any, is not yet understood. According to one researcher in the area, "no ingredient [constituent] or group of ingredients [constituents] as found in tobacco smoke have been established as disease producing in smokers."[1]

II. SMOKE CONSTITUENTS

A. "Tar"

"Tar" is an artificially created laboratory product consisting of highly concentrated and physically altered cigarette smoke particulate matter which is gathered either by passing cigarette smoke through a cold trap at extremely low temperatures or by using filters and a drying process. The substances as found in "tar" are not found in cigarette smoke. That may be why this product is sometimes referred to as condensate. Certainly, material collected in this way does not duplicate what humans are exposed to when they smoke. As a report on a meeting of experts in the area noted:

> [T]here is, at present, no available instrumentation permitting the separation and

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individual collection of the particulate and gas phases which duplicates the precise physico-chemical conditions prevailing in cigarette smoke as it is inhaled.[2]

Despite its apparent lack of relevance to smoking, laboratory-produced "tar" has been used in animal experiments designed to investigate the possible relationship between tobacco smoke and cancer. In those experiments, "tar" was repeatedly painted on the shaved backs or ears of test animals over prolonged periods of time. These so-called skin-painting experiments have prompted a great deal of interest, as the tumors which resulted have been said to be evidence that tumors might develop in human lungs from inhaling cigarette smoke.

The results of such animal experiments cannot and should not be extrapolated to the human situation. Even if the "tar" collected by the methods described above were present in cigarette smoke, the "tar" used in skin painting experiments is very different by the time it is studied in the laboratory. That is because after "tar" is collected, it continues to undergo chemical changes as long as it is stored.[3] Furthermore, as an experimental toxicologist has noted, <u>even if</u> an effect such as tumor production is observed in a particular species, that does not necessarily mean that it might "occur either quantitatively or qualitatively in man."[4]

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Skin painting experiments suffer from a number of additional weaknesses. For example, the concentrations of "tar" used in such experiments are extremely high. It has been estimated that the amounts utilized would be equivalent to an individual smoking over 100,000 cigarettes per day.[5] Furthermore, the skin and ears of laboratory animals are not similar to human lung tissue. Animal skin lacks the intricate clearance mechanisms of the lungs, such as the mucus blanket which coats the lining of the major airways of the lung. Even the summary report of a study sponsored by the United States government utilizing skin painting techniques conceded "the uncertain relationship between tumors resulting from mouse skin painted with condensate and human lung cancer."[6] Consequently, such experiments have been characterized as involving applying "the wrong material in the wrong form, in the wrong dosage, to the wrong tissue of the wrong animal."[7]

It is misleading, therefore, to draw definitive conclusions about "tar" and human disease from skin painting studies. As a knowledgeable observer of research in this area has stated: "Bronchogenic carcinoma [lung cancer] has never been produced by tobacco or its products in any experimental animal despite the multiplicity of attempts."[8] (Emphasis added) All in all, the following statement made in the mid-1970's still provides a concise summary of the current state of scientific data concerning "tar":

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Human beings do not smoke 'tar' and laboratory reports on 'tar' yields have not been established as significant to human health.[9]

B. Nicotine

Nicotine is a natural element of tobacco and, thus, is present in tobacco smoke. Nicotine has been described by some researchers as having no known chronic or cumulative effects on human health.[10] The data on the nature of nicotine's relationship to human health is inconclusive at best, because, among other things, science cannot determine with any precision how much nicotine a smoker is exposed to. In fact, no correlation between the nicotine level of a cigarette or the number of cigarettes smoked and the smoker's actual nicotine intake has been conclusively established because of individual variations in puff rates, depth of inhalation, and body metabolism.[11]

Nonetheless, anti-smoking advocates blame nicotine for the development of heart disease. Yet no biological mechanism by which nicotine, or any other agent, may be involved in heart disease has been demonstrated. Serious questions about what role, if any, nicotine plays have been raised as a result of autopsy findings of fatty deposits and other changes in the arteries of individuals who either have not smoked or could have smoked only briefly, such as infants, children, and young men killed in military battle.[12] Even the 1983 U.S. Surgeon General's Report, which focused on car-

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diovascular disease, concedes that "the evidence for and against a primary role for nicotine in the development or acceleration of atherosclerosis is not conclusive. . . ."[13] That opinion was shared by a German researcher who has conducted research on the relationship between nicotine and the clogging of arteries. After reviewing the literature, he and his co-author concluded that "there is no established evidence which supports the hypothesis that nicotine has any influence on the development" of those changes.[14] (Emphasis added)

Claims by anti-smoking advocates regarding the role of nicotine in the development of heart disease are further undermined by two epidemiological (population) studies. In a study that dealt with myocardial infarction (heart attack), the authors reported finding -- contrary to what they expected -- that the nicotine and carbon monoxide levels of the cigarettes their subjects smoked were not related to the risk of heart attack.[15]

The second study, chaired by a well-known British scientist opposed to cigarette smoking, examined the serum (blood) levels of cotinine, a nicotine metabolite, in male nonsmokers and smokers of cigarettes only, cigars only, and pipes only. The study determined that the mean cotinine level for pipe smokers was significantly higher than the levels for cigarette and cigar smokers. Since studies of pipe smokers generally have not reported an increased risk of coronary heart disease, the researchers concluded

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that "nicotine is unlikely to be the major cause of the excess coronary heart disease mortality in cigarette smokers."[16] After re-evaluating their methodology in response to anti-smoking criticism of their study, the researchers again concluded that they were "reasonably confident" that "exposure to high systemic concentrations of nicotine is not a cause of the disease." Although the researchers quibbled with the result of their own study, arguing that their data "cannot completely exonerate" nicotine, they added that the data do "substantially reduce the weight of evidence suggesting that nicotine is a cause of coronary heart disease."[17]

Animal studies which purport to establish a causal role for nicotine in heart disease have been soundly criticized for their unrealistic and excessive test conditions. An American researcher who conducted animal studies on this subject has noted:

> There have been some studies that have exhibited minor or questionable changes with the use of an equivalent dose of 600 or more cigarettes a day in man. This is such a large number that I think man would find it difficult to find the time to smoke them.[18]

In contrast, this researcher concluded that animal studies using realistic doses of nicotine have "failed to initiate, exacerbate, or otherwise influence" the process leading to the clogging of arteries in test animals.[19] In one such study, which was funded by the United States government, male beagle dogs fed a special diet to induce this process were exposed for two years to cigarette

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smoke containing low or high levels of nicotine and, in some cases, enriched with carbon monoxide. According to the final report of the research laboratory which conducted the study, "the results of this study lent no support to the suggestion that cigarette smoking increases the rate of development" of this process.[20]

The foregoing demonstrates the validity of one researcher's summary: "While many studies have been done in this field, none have established nicotine as contributing to the causation, aggravation or precipitation of any cardiovascular disease."[21] (Emphasis added)

C. Carbon Monoxide

Carbon monoxide (CO) is a tasteless, odorless, colorless gas produced by many natural and man-made sources, including automobile exhaust and industrial emissions. It is naturally produced by the body during daily metabolism. Burning cigarettes also produce CO, but that amount has been described as "insignificant" compared to most other sources.[22] Nonetheless, CO has received considerable attention in the scientific literature, usually in regard to cardiovascular disease (CVD). In a review of such literature, however, two public health specialists concluded that "despite the large amount of literature available, the conclusions that can be drawn as to the role of CO in human CVD remain tentative and open to varying interpretations."[23] This conclusion is supported

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by a similar statement in the 1983 U.S. Surgeon General's Report, which focused on heart disease:

> Carbon monoxide is another major component of cigarette smoke for which there are some data supporting a possible atherogenic [plaque forming inside the arteries] role; however, a review of recent literature on the role of carbon monoxide in arterial injury and atherogenesis leads to no consensus.[24]

The conclusion of another group which also reviewed the literature was more concise. The chairman of the American Heart Association Task Force on Environment and the Cardiovascular System reported that his group had concluded that the question of whether CO causes heart disease "remains unanswered even at the basic science level."[25] (Emphasis added)

Specialists who reviewed these and other studies have concluded that "there is no evidence" to support the suggestion that exposure to low or moderate levels of CO increases the rate of development of atherosclerotic disease in man. Indeed, they contend that "sufficient evidence is available to support the conclusion that, in fact, CO is not of pathogenetic [disease causing] consequence in atherosclerotic disease."[26] (Emphasis added)

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D. Other Constituents*

Over the years, the principal focus of the attention and concern of smoking critics has been on "tar," nicotine and CO. One researcher who has tried to establish a causal link between smoking and disease, however, concluded with reference to these substances that:

> We assume that it is the tar which causes lung cancer, but we do not know this for certain.
>
> Until now, we have implicated nicotine in the development of cardiovascular diseases, but we cannot prove this.
>
> The same is true for CO.[27]

Thus, some anti-smoking advocates have attempted to shift public attention to the presence of other substances in cigarette smoke. These substances, as found in cigarette smoke (like "tar," nicotine, and CO), have not been scientifically proven to cause any disease in humans. Nonetheless, these constituents are of interest because at levels and under conditions of exposure greatly different than those encountered by the smoker, certain of these compounds may have a toxic effect on or may be associated with disease in animals or humans.

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* A more detailed discussion of specific constituents appears in Appendix A to this paper.

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It is an axiom among toxicologists that any substance is toxic if the level of exposure is high enough and no substance is toxic if the level of exposure is low enough.[28] The amount of substances other than nicotine and CO in cigarette smoke is extremely low, measured in terms of micrograms and nanograms per cigarette. As previously noted, a microgram is one-millionth of a gram, the equivalent of one second in twelve days. A nanogram is one billionth of a gram, the equivalent of one second in thirty-two years.

Moreover, these substances are for the most part natural by-products of combustion of any organic matter, including tobacco, or are found in any organic matter whether or not that matter is burned. Likewise, other compounds present in smoke are also present in the air we breathe and the water we drink. Thus, it is scientifically inaccurate to state as "fact" that there is something "unique" about the presence of these substances in cigarette smoke.

III. CONCLUSION

Numerous claims have been made about the relationship between cigarette smoke constituents and the health of the smoker. However, such claims are just that -- claims which are not supported by reliable scientific proof. After years of study, no scientific relationship has been established between "tar," nicotine and carbon monoxide and human disease. Other constituents, detectable at extremely low levels in cigarette smoke, are the subject of occa-

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sional public comment. These substances are not unique to tobacco smoke, however, and as with "tar," nicotine and CO, have not been proven to cause disease in humans in the form in which they are found in cigarette smoke.

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